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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/091,561	08/21/98	PLOUET	USB95ARCNR

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EXAMINER
EWOLDT,G

ART UNIT	PAPER NUMBER
1644	10

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/091,561	Applicant(s) Plouet et al.
	Examiner Gerald Ewoldt	Group Art Unit 1644

☒ Responsive to communication(s) filed on *Mar 8, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *18-35* is/are pending in the application.

Of the above, claim(s) *18-24 and 31* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *25-30 and 32-35* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *10*

☐ Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's election with traverse of Group IV, claims 25-30 and 32-35 in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the restriction is improper under PCT Rule 13. Applicant finds the argument of using prior art against a single group to establish the lack of a special technical feature "bewildering" but continues by arguing against the art cited. Applicant finds the conclusions drawn based on the art "fundamentally mistaken" and "baseless". Applicant finds separation of different methods into separate groups "incredible" and finds the citing of MPEP Chapter 800 "improper". Applicant asserts that because no lack of unity was found during the International Phase an "undue searching burden" cannot now be "contended". Finally, Applicant notes that "separate classification (of groups) is no evidence whatsoever of the propriety of a restriction requirement". This is not found persuasive because:

A) The use of prior art against an independent claim is one method of establishing a lack of unity. The prior art need not teach every limitation of every claim, but only the technical feature common to all the claims. Absent a special (novel or unobvious) technical feature common to all the claimed inventions there is a lack of unity. In the instant case the technical feature common to all the claims is an anti-idiotype VEGF antibody as in Group IV.

B) Applicant fails to argue that U.S. Patent No. 5,942,385 is not prior art. Instead, Applicant argues that the U.S. filing date is subsequent to the French priority date. As Applicant has not supplied an English translation of the priority document in a timely manner, the French priority date cannot be granted for restriction purposes.

C) Applicant argues that the Plouet et al. reference does not teach all the limitations of the instant application. Applicant is reminded that the prior art reference need only teach the technical feature of any claimed invention, i.e. the antibody used in the method of claim 18, and not all the limitations disclosed in the specification,

i.e., antibody internalization and flk vs. flt binding.

D) The methods of Groups I-III have not been restricted because of scope differences, as argued by Applicant, but rather because they are patentably distinct, i.e., the methods of Group II and III are mutually exclusive and therefore patentably distinct.

E) Applicant is correct in the assertion that references to restriction under MPEP Chapter 800 are improper, however, the groupings under lack of unity of invention and the reasons for said groupings would be the same and therefore remain proper.

F) As Applicant points out, U.S. restriction practice does not apply to the instant case, therefore the arguments against searching burden and U.S. classification differences also do not apply.

G) Additionally, as unity of invention practice, and not U.S. restriction practice, applies to cases filed under 35 U.S.C. 371, Applicant is reminded that unity of invention between different categories of inventions will only be found to exist if specific combinations of inventions are present. The allowed combinations do not include multiple methods of using a product as claimed in the instant application, see MPEP § 1850.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 18-24 and 31 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 25-30 and 32-35 are being acted upon.

3. Formal drawings have been submitted which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948. Applicant is reminded to change the Brief Description of the Drawings in accordance with these changes.

4. The disclosure is objected to because of the following informalities:

A) Figure 5 contains no legend and is thus indecipherable.

B) The specification contains no figure labeled "Figure 6".

C) Page 14, line 10, of the specification, "The conditioned medium (30 liters) was purified as described above" has no description of a medium purification process preceding it.

D) Page 19, line 28, "ACE cells" have not been defined.

E) Page 20, line 28, hypotension has been misspelled.

F) the term "trigger off", used repeatedly throughout the specification, i.e., page 23, line 28, is considered to be slang for induce but must be defined.

Appropriate correction is required.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 29-30 and 32-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

A) Regarding claims 29 and 30, the phrase "in particular" renders the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

B) Regarding claim 29, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

C) Regarding claim 30, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

D) Regarding claim 30, the phrase "possible" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

E) Regarding claim 30, the phrase "above-mentioned" renders the claim indefinite. The proper word is "said".

F) Regarding claim 32-35, the use of the plural "compositions" renders the claims indefinite. Proper usage is to claim the singular "composition".

G) Regarding claims 32-35, the phrase "active substance" renders the claims indefinite because the meaning of "active substance" has not been defined in the specification.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 37(C) of this title before the invention thereof by the applicant for patent.

9. Claims 25, 30, and 32 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Plouet et al. (1994, IDS).

Plouet et al. teach an anti-idiotypic VEGF antibody. While the reference does not teach that the antibody is a ligand for KDR or flk-1 and not a ligand for flt, it would be an inherent property given that: 1) the antibodies were produced in the same way and, 2) KDR and flk-1 are less than 50% homologous with flt. It would be extremely unlikely that an antibody *could* be an a ligand for KDR and flt-1 and flk. Additionally, the reference antibody displays the same *in vivo* property as the claimed antibody in that both stimulate prostatic tumor growth

(see particularly paragraphs 1-2). Claim 30 is included in the rejection because the process by which the antibody is produced lends no patentable weight to the invention. Claim 32 is included in the rejection because the abstract includes *in vivo* data (paragraph 2) thus indicating a pharmaceutical composition.

The reference teaching clearly anticipates the claimed invention.

10. Claims 25-28, 30, and 32-34 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by U.S. Patent No. 5,942,385 (1999).

The '385 patent teaches an anti-idiotypic VEGF antibody and epitope binding (Fab) fragments of said antibody (see particularly column 8, paragraph 6). While the reference does not teach that the antibody or Fab fragments thereof are ligands for KDR or flk-1 and not ligands for flt, it would be an inherent property for the reasons described supra. Claim 26 is included in the rejection because the antibody of the '385 patent would inherently possess the properties of the claimed antibody. Claim 30 is included in the rejection because the process by which the antibody is produced lends no patentable weight to the invention. Claims 32-34 are included in the rejection because the reference teaches the use of the antibody and fragments thereof *in vivo* thus indicating a pharmaceutical composition.

The reference teaching clearly anticipates the claimed invention.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Plouet et al. in view of Kieber-Emmons et al. (1986).

Plouet et al. has been discussed supra. The reference teaching differs from the claimed in that it does not teach Fab fragments of the anti-idiotypic VEGF antibody.

Kieber-Emmons et al. teaches that Fab fragments possess the binding capacity and thus functional activity of whole anti-idiotypic antibodies (see particularly page 2, paragraphs 3-4).

From the teachings of the references it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make just the Fab fragments, as taught by Kieber-Emmons et al., of an anti-idiotype VEGF antibody, as taught by Plouet et al. One of ordinary skill in the art at the time the invention was made would have been motivated to produce said Fab fragments because they retain the binding capacity and thus functional activity of whole anti-idiotypic antibodies, as taught by Kieber-Emmons et al.

13. Claims 29 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Plouet et al. or U.S. Patent No. 5,942,385 each in view of U.S. Patent No. 4,792,447 or U.S. Patent No. 4,737,453.

Plouet et al. and the '385 patent have been discussed supra. The references differ from the claimed invention only in that they do not teach a complex of the anti-idiotype VEGF antibody with a toxin (such as ricin) or a radioactive element.

The '447 patent teaches a complex of an anti-idiotypic antibody with ricin thus "providing (a) site-specific immunotherapeutic agent". (see particularly column 5, paragraph 5 and column 4, paragraph 1).

The '453 patent teaches a complex of an antibody or Fab fragment with iodine-125 (see particularly column 4, paragraph 5)

From the teachings of the references it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make an anti-idiotype VEGF antibody, as taught by

Plouet et al. or the '385 patent, complexed with ricin, as taught by the '447 patent, or iodine-125, as taught by the '453 patent. One of ordinary skill in the art at the time the invention was made would have been motivated to produce said antibody-ricin complex to create a "site-specific immunotherapeutic agent", as taught by the '447 patent, for targeting endothelial cells, as taught by Plouet et al. or the '385 patent, or an antibody-iodine-125 complex, as taught by the '453 patent.

14. No claim is allowed.

15. The Ortega et al. reference has been considered as far as discussed in the English translation of the Abstract only.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Friday from 8:00 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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